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Application Number

09/782,721

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February 12, 2001

First Named Inventor

H. Michael SHEPARD

Art Unit

1623 -4653-

Examiner Name

L. Crane

Attorney Docket Number

NB 2004.02

## U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code <sup>2</sup> (if known)			
<i>me</i>	1	US-4,247,544	01-27-81	Bergstrom, et al.	
<i>me</i>	2	US-4,267,171	04-12-81	Bergstrom, et al.	
<i>me</i>	3	US-4,542,210	09-17-85	Sakata et al.	
<i>me</i>	4	US-4,816,570	03-28-89	Farquhar	
<i>me</i>	5	US-4,948,882	08-14-90	Ruth	
<i>me</i>	6	US-4,975,278	12-04-90	Senter et al.	
<i>me</i>	7	US-5,085,983	02-04-92	Scanlon	
<i>me</i>	8	US-5,233,031	08-03-92	Borch et al.	
<i>me</i>	9	US-5,264,618	11-23-93	Felgner et al.	
<i>me</i>	10	US-5,459,127	10-17-85	Felgner et al.	
<i>me</i>	11	US-5,521,161	05-28-96	Malley et al.	
<i>me</i>	12	US-5,627,165	05-06-97	Glazier	
<i>me</i>	13	US-5,645,988	07-08-97	Vande Woude et al.	
<i>me</i>	14	US-5,663,321	09-02-97	Gmeiner et al.	
<i>me</i>	15	US-5,798,340	08-25-98	Bischofberger et al.	
<i>me</i>	16	US-5,981,507	11-09-99	Josephson et al.	

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## FOREIGN PATENT DOCUMENTS

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<del>AA</del>	17	<del>GB 982 776</del>	02/10/65	The Wellcome Foundation		
<i>me</i>	18	WO 91/17424	11/14/91	Vical, Inc.		
<i>me</i>	19	WO 94/03467	02/17/94	Institute of Organic Chemistry & Biochemistry of the Academy of Sciences of the Czech Republic, Rega Stichting VZW and Gilead Sciences, Inc.		
<i>me</i>	20	WO 96/29336	06/26/96	Amersham International, PLC		
<i>me</i>	21	WO 96/40088	12/19/96	Hostettler, Karl		
<del>AA</del>	22	<del>WO 97/28179</del>	<del>08/07/97</del>	Fick, James & Israel, Mark		

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Applicati n Numb r	09/782,721
Filing Date	February 12, 2000
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Art Unit	1623 -1653 --
Examiner Name	L. Crane
Attorney Docket Number	NB 2004.02

## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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Me	24 !	Abraham et al., "Synthesis and biological activity of aromatic amino acid phosphoramidates of 5-fluoro-2'-deoxyuridine and 1-J-arabinofuranosylcytosine: Evidence of phosphoramidase activity" <i>J. Med. Chem.</i> 39:4569-4575 (1996).	
Me	25 !	Akdas et al., "Glutathione S-transferase and multidrug-resistant phenotype in transitional cell carcinoma of the bladder" <i>Eur. Urol.</i> 29(4):483-486 (1996).	
Me	26 !	Almasan et al., "Genetic instability as a consequence of inappropriate entry into and progression through S-phase" <i>Can. Metastasis Rev.</i> 14:59-73 (1995).	
Me	27 !	Andersen et al., "Detection of c-erbB-2 related protein in sera from breast cancer patients" <i>Acta Oncol.</i> 34(4):499-504 (1995).	
Me	28 !	Anglada et al., "N,N-cyclization of carbodiimides with 2-(bromomethyl)acrylic acid. A direct entry to the system 5-methylene-6H-pyrimidine-2,4-dione, A new class of thymine analogues" <i>J. Heterocycl. Chem.</i> 33:1259-1270 (1996).	
Me	29 !	Antelman et al., "Inhibition of tumor cell proliferation <i>in vitro</i> and <i>in vivo</i> by exogenous p110RB, the retinoblastoma tumor suppressor protein" <i>Oncogene</i> 10:697-704 (1995).	
Me	30 !	Asakura et al., "Cerium(IV) catalyzed iodination at C5 of uracil nucleosides" <i>Tetrahedron Lett.</i> 29(23):2855-2858 (1988).	
Me	31 !	Asakura et al., "Cerium(IV)-mediated halogenation at C-5 of uracil derivatives" <i>J. Org. Chem.</i> 55:4928-4933 (1990).	
Me	32 !	Ayisi et al. "Comparison of the antiviral effects of 5-methoxymethyldeoxyuridine-5'-monophosphate with adenine arabinoside-5'-monophosphate" <i>Antivirals Res.</i> 3:161-174 (1983)	
Me	33 !	Balzarini et al., "Incorporation of 5-substituted pyrimidine nucleoside analogues into DNA of a thymidylate synthetase-deficient murine FM3A carcinoma cell line" <i>Meth. Find. Exp. Clin. Pharmacol.</i> 7(1):19-28 (1985).	
Me	34 !	Balzarini, J. et al., "Thymidylate synthase is the principal target enzyme for the cytostatic activity of (E)-5-(2-bromovinyl)-2'-deoxyuridine against murine mammary carcinoma (FM3A) cells transformed with the herpes simplex virus type 1 or type 2 thymidine kinase gene" <i>Mol. Pharmacol.</i> 32:410-416 (1987).	
Me	35 !	Balzarini et al., "Differential mechanism of cytostatic effect of (E)-5-(2-bromovinyl)-2'-deoxyuridine, 9-(1,3-dihydroxy-2-propoxymethyl)guanine, and other antiherpetic drugs on tumor cells transfected by the thymidine kinase gene of herpes simplex virus type 1 or type 2" <i>J. Biol. Chem.</i> 268(9):6332-6337 (1993).	
Me	36 !	Balzarini et al., "Anti-HIV and anti-HBV activity and resistance profile of 2',3'-dideoxy-3'-thiacytidine (3TC) and its arylphosphoramidate derivative CF 1109" <i>Biochem. Biophys. Res. Commun.</i> 225:363-369 (1996).	
Me	37 !	Balzarini et al., "Conversion of 2',3'-dideoxyadenosine (ddA) and 2',3'-dideoxy-2',3'-dideoxyadenosine (d4A) to their corresponding arylphosphoramidate derivatives markedly potentiates their activity against human immunodeficiency virus and hepatitis B virus" <i>FEBS Lett.</i> 410:324-328 (1997).	
Me	38 !	Banerjee et al., "Molecular mechanisms of resistance to antifolates, a review" <i>Acta Biochem. Pol.</i> 42(4):457-464 (1995).	
Me	39 !	Banerjee et al., "Role of E2F-1 in chemosensitivity" <i>Can. Res.</i> 58:4292-4296 (1998).	
Me	40 !	Barbour et al., "A naturally occurring tyrosine to histidine replacement at residue 33 of human thymidylate synthase confers resistance to 5-fluoro-2'-deoxyuridine in mammalian and bacterial cells" <i>Mol. Pharmacol.</i> 42:242-248 (1992).	
Me	41 !	Barr, "Inhibition of thymidylate synthetase by 5-alkynyl-2'-deoxyuridylates" <i>J. Med. Chem.</i> 24(12):1385-1388 (1981).	
Me	42 !	Barr et al., "Thymidylate synthetase-catalyzed conversions of E-5-(2-bromovinyl)-2'-deoxyuridylate" <i>J. Biol. Chem.</i> 258(22):13627-13631 (1983).	
Me	43 !	Barr et al., "Reaction of 5-ethynyl-2'-deoxyuridylate with thiols and thymidylate synthetase" <i>Biochem.</i> 22:1696-1703 (1983).	
Me	44 !	Barrett, "Trapping of the C5 methylene intermediate in thymidylate synthase" <i>J. Am. Chem. Soc.</i> 120:449-450 (1998).	
Me	45 !	Benzaria et al., "Synthesis, <i>in vitro</i> antiviral evaluation, and stability studies of bis(S-acyl-2-thioethyl) ester derivatives of 9-[2-(phosphonomethoxy)ethyl]adenine (PMEA) as potential PMEA prodrugs with improved oral bioavailability" <i>J. Med. Chem.</i> 39:4958-4965 (1996).	
Me	46 !	Bergstrom et al., "C-5-substituted pyrimidine nucleosides. 3. Reaction of allylic chlorides, alcohols, and acetates with pyrimidine nucleoside derived organopalladium intermediates" <i>J. Org. Chem.</i> 46(7):1432-1441 (1981).	
Me	47 !	Bergstrom et al., "Synthesis of (E)-5-(3,3,3-trifluoro-1-propenyl)-2'-deoxyuridine and related analogues: Potent and unusually selective antiviral activity of (E)-5-(3,3,3-trifluoro-1-propenyl)-2'-deoxyuridine against herpes simplex virus type 1" <i>J. Med. Chem.</i> 27:279-284 (1984).	
Me	48 !	Bertino et al., "Resistance mechanisms to methotrexate in tumors" <i>Stem Cells</i> 14:5-9 (1996).	

! Month of publication data is unavailable for this citation.

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## OTHER PRIOR ART - NON-PATENT LITERATURE DOCUMENTS

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JAL	49 !	Bigge et al., "Palladium-catalyzed coupling reactions of uracil nucleosides and nucleotides" <i>J. Amer. Chem. Soc.</i> 102:2033-2038 (1980).	
JAL	50 !	Bosslet et al., "A novel one-step tumor-selective prodrug activation system" <i>Tumor Targeting</i> 1:45-50 (1995).	
JAL	51 !	Bosslet et al., "Elucidation of the mechanism enabling tumor selective prodrug monotherapy" <i>Can. Res.</i> 58:1195-1201 (1998).	
JAL	52 !	Brisson, "Gene amplification and tumor progression" <i>Biochem. Biophys. Acta</i> 1155:25-41 (1993).	
JAL	53 !	Carl et al., "Protease-activated 'prodrugs' for cancer chemotherapy" <i>PNAS USA</i> 77(4):2224-2228 (1980).	
JAL	54 !	Carreras et al., "The catalytic mechanism and structure of thymidylate synthase" <i>Ann. Rev. Biochem.</i> 64:721-762 (1995).	
JAL	55 !	Carter et al., "Humanization of an anti-p185HER2 antibody for human cancer therapy" <i>PNAS USA</i> 89:4285-4289 (1992).	
JAL	56 !	Cava et al., "Thionation reactions of lawesson's reagents" <i>Tetrahedron</i> 41(22):5061-5087 (1985).	
JAL	57 !	Chakravarty et al., "Plasmin-activated prodrugs for cancer chemotherapy. 2. Synthesis and biological activity of peptidyl derivatives of doxorubicin" <i>J. Med. Chem.</i> 26(5):638-644 (1983).	
JAL	58 !	Chaudhuri et al., "Very high affinity DNA recognition by bicyclic and cross-linked oligonucleotides" <i>J. Am. Chem. Soc.</i> 117:10434-10442 (1995).	
JAL	59 !	Chen et al., "Sensitization of human breast cancer cells to cyclophosphamide and ifosfamide by transfer of a liver cytochrome P450 gene" <i>Can. Res.</i> 56:1331-1340 (1996).	
JAL	60 !	Cho et al., "(E)-5-(3-oxopropen-1-yl)-2'-deoxyuridine and (E)-5-(3-oxopropen-1-yl)-2',3'-dideoxyuridine; New antiviral agents: Synthesis and biological activity" <i>Tetrahedron Lett.</i> 35(8):1149-1152 (1994).	
JAL	61 !	Clarke, "Animal models of breast cancer: Their diversity and role in biomedical research" <i>Breast Can. Res. Treat.</i> 39:1-6 (1996).	
JAL	62 !	Colacino, "Mechanisms for the anti-hepatitis B virus activity and mitochondrial toxicity of fialuridine (FIAU)" <i>Antiviral Res.</i> 29:125-139 (1996).	
JAL	63 !	Collins, J.M. et al. "Suicide prodrugs activated by Thymidylate synthase: Rationale for treatment and noninvasive imaging of tumors with deoxyuridine analogues" <i>Clin. Cancer Res.</i> 5:1976-1981 (August 1999)	
JAL	64 !	Connors, "Prodrugs in cancer chemotherapy" <i>Xenobiotica</i> 16(10/11):975-988 (1986).	
JAL	65 !	Connors, et al., "Prodrugs in cancer chemotherapy" <i>Stem Cells</i> 13:501-511 (1995).	
JAL	66 !	Connors, "Is there a future for cancer chemotherapy?" <i>Annals Oncol.</i> 7:445-452 (1996).	
JAL	67 !	Copur et al., "Thymidylate synthase gene amplification in human colon cancer cell lines resistant to 5-fluorouracil" <i>Biochem. Pharmacol.</i> 49(10):1419-1426 (1995).	
JAL	68 !	Crisp, "Synthesis of 5-alkenyl-2'-deoxyuridines via organostannanes" <i>Synth. Commun.</i> 19(11 & 12):2117-2123 (1989).	
JAL	69 !	Dale et al., "The synthesis and enzymatic polymerization of nucleotides containing mercury: Potential tools for nucleic acid sequencing and structural analysis" <i>PNAS USA</i> 70(8):2238-2242 (1973).	
JAL	70 !	Davisson et al., "Expression of human thymidylate synthase in <i>Escherichia coli</i> " <i>J. Biol. Chem.</i> 264(16):9145-9148 (1989).	
JAL	71 !	Davisson et al. "Expression of human thymidylate synthase in <i>Escherichia coli</i> . (Additions and corrections)" <i>J. Biol. Chem.</i> 269(48):30740 (1994).	
JAL	72 !	De Clercq et al., "Nucleic acid related compounds. 40. Synthesis and biological activities of 5-alkynyluracil nucleosides" <i>J. Med. Chem.</i> 26:661-666 (1983).	
JAL	73 !	Dicker et al., "Methotrexate resistance in an in vivo mouse tumor due to a non-active-site dihydrofolate reductase mutation" <i>PNAS USA</i> 90:11797-11801 (1993).	
JAL	74 !	Dirven et al., "The role of human glutathione S-transferase isoenzymes in the formation of glutathione conjugates of the alkylating cytostatic drug thiotepa" <i>Can. Res.</i> 55:1701-1706 (1995).	
JAL	75 !	Dorr et al., "PALA" In: <i>Cancer Chemotherapy Handbook</i> : Appleton & Lange, Norwalk, Connecticut:768-773 (1994).	
JAL	76 !	Dunn et al., "Solution of the conformation and alignment tensors for the binding of trimethoprim and its analogs to dihydrofolate reductase: 3D-quantitative structure-activity relationship study using molecular shape analysis, 3-way partial least-squares regression, and 3-way factor analysis" <i>J. Med. Chem.</i> 39:4825-4832 (1996).	
JAL	77 !	Dyer et al., "Nucleic Acids Chemistry: Improved and new synthetic procedures, methods, and techniques" Townsend, L. B. & Tipson, R. S., eds. (Wiley-Interscience, New York, NY) Vol. 4:79-83 (1991).	
JAL	78 !	Eccles et al., "Significance of the c-erbB family of receptor tyrosine kinases in metastatic cancer and their potential as targets for immunotherapy" <i>Invasion Metastasis</i> 14(1-6):337-348 (1994-95).	
JAL	79 !	Eisenbrand et al., "An approach towards more selective anticancer agents" <i>J. Synthetic Organic Chem.</i> 10:1246-1258 (1996).	
JAL	80 !	Evad, A. et al. "An in vitro nucleoside analog screening method for cancer gene therapy" <i>Chem. Abstracts</i> 126:Abstract No. 26514 (1996)	
JAL	81 !	Farquhar et al., "Synthesis and antitumor evaluation of bis[(pivaloyloxy)methyl] 2'-deoxy-5-fluorouridine 5'-monophosphate (FdUMP): A strategy to introduce nucleotides into cells" <i>J. Med. Chem.</i> 37:3902-3909 (1994).	
JAL	82 !	Farquhar et al., "5'-[4-pivaloyloxy]-1,3,2-dioxaphosphorinan-2-yl]-2'-deoxy-5-fluorouridine: A membrane-permeating prodrug of 5-fluoro-2'-deoxyuridylic acid (FdUMP)" <i>J. Med. Chem.</i> 38:488-495 (1994).	
JAL	83 !	Felip et al., "Overexpression of c-erbB-2 in epithelial ovarian cancer" <i>Cancer</i> 75(8):2147-2152 (1995).	
JAL	84 !	Finch et al., "Radiation Injury" In: <i>Harrison's Principles of Internal Medicine</i> , 12th edition: McGraw-Hill, Inc., New York, NY:2204-2208 (1991).	

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## OTHER PRIOR ART - NON-PATENT LITERATURE DOCUMENTS

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Jee	85	Finer-Moore et al., "Refined structures of substrate-bound and phosphate-bound thymidylate synthase from <i>Lactobacillus casei</i> " <i>J. Mol. Biol.</i> 232:1101-1116 (1993).	
Jee	86	Finer-Moore et al., "Crystal structure of thymidylate synthase from T4 phage: Component of a deoxynucleoside triphosphate-synthesizing complex" <i>Biochem.</i> 33:15459-15468 (1994).	
Jee	87	Firestone et al., "A comparison of the effects of antitumor agents upon normal human epidermal keratinocytes and human squamous cell carcinoma" <i>Chem Abstracts</i> 113:Abstract No. 254 (1990)	
Jee	88	Freed et al., "Evidence for acyloxymethyl esters of pyrimidine 5'-deoxyribonucleotides as extracellular sources of active 5'-deoxyribonucleotides in cultured cells" <i>Biochem. Pharmacol.</i> 38(19):3193-3198 (1989).	
Jee	89	Fries et al., "Synthesis and biological evaluation of 5-fluoro-2'-deoxyuridine phosphoramidate analogs" <i>J. Med. Chem.</i> 38(14):2672-2680 (1995).	
Jee	90	Garrett et al., "Thymidylate synthetase. Catalysis of dehalogenation of 5-bromo- and 5-iodo-2'-deoxyuridylate" <i>Biochem.</i> 18(13):2798-2804 (1979).	
Jee	91	Goldberg et al., "Novel cell imaging techniques show induction of apoptosis and proliferation in mesothelial cells by asbestos" <i>Am. J. Respir. Cell Mol. Biol.</i> 17:265-271 (1997)	
Jee	92	Goldstein et al., "Genetic aspects of disease" In: Harrison's Principles of Internal Medicine, 12th edition: McGraw-Hill, Inc., New York, NY:21-76 (1991).	
Jee	93	Goodwin et al., "Incorporation of alkylthiol chains at C-5 of deoxyuridine" <i>Tetrahedron Lett.</i> 34(35):5549-5552 (1993).	
Jee	94	Gottesman et al., "Genetic analysis of the multidrug transporter" <i>Ann. Rev. Gen.</i> 29:607-649 (1995).	
Jee	95	Graham et al., "DNA duplexes stabilized by modified monomer residues: Synthesis and stability" <i>J. Chem. Soc. Perkin Trans.</i> 1:1131-1138 (1998).	
Jee	96	Gros et al., "Isolation and expression of a complementary DNA that confers multidrug resistance" <i>Nature</i> 323:728-731 (1986).	
Jee	97	Gros et al., "Mammalian multidrug resistance gene: Complete cDNA sequence indicates strong homology to bacterial transport proteins" <i>Cell</i> 47:371-380 (1986).	
Jee	98	Gros et al., "Isolation and characterization of DNA sequences amplified in multidrug-resistant hamster cells" <i>PNAS USA</i> 83:337-341 (1986).	
Jee	99	Gudkov et al., "Cloning and characterization of DNA sequences amplified in multidrug-resistant djungarian hamster and mouse cells" <i>Somat. Cell Mol. Genet.</i> 13(6):609-619 (1987).	
Jee	100	Hardy et al., "Atomic structure of thymidylate synthase: Target for rational drug design" <i>Science</i> 235:448-455 (1987).	
Jee	101	Harris et al., "Adenovirus-mediated p53 gene transfer inhibits growth of human tumor cells expressing mutant p53 protein" <i>Can. Gene Ther.</i> 3(2):121-130 (1996).	
Jee	102	Hashimoto et al., "Simple separation of tritiated water and [3H] deoxyuridine from [5-3H] deoxyuridine 5'-monophosphate in the thymidylate synthase assay" <i>Anal. Biochem.</i> 167:340-346 (1987).	
Jee	103	Hengstschläger et al., "The role of p16 in the E2F-dependent thymidine kinase regulation" <i>Oncogene</i> 12:1635-1643 (1996).	
Jee	104	Hobbs, "Palladium-catalyzed synthesis of alkynylamino nucleosides. A universal linker for nucleic acids" <i>J. Org. Chem.</i> 54:3420-3422 (1989).	
Jee	105	Horikoshi et al., "Quantitation of thymidylate synthase, dihydrofolate reductase, and DT-diaphorase gene expression in human tumors using the polymerase chain reaction" <i>Can. Res.</i> 52:108-116 (1992).	
Jee	106	Horn et al., "Fialuridine is phosphorylated and inhibits DNA synthesis in isolated rat hepatic mitochondria" <i>Antiviral Res.</i> 34:71-74 (1997).	
Jee	107	Hostettler et al., "Enhanced oral absorption and antiviral activity of 1-o-octadecyl-sn-glycero-3-phospho-acyclovir and related compounds in hepatitis B virus infection, <i>in vitro</i> " <i>Biochem. Pharmacol.</i> 53:1815-1822 (1997).	
Jee	108	Houze, "Detection of thymidylate synthase gene expression levels in formalin-fixed paraffin embedded tissue by semiquantitative, nonradioactive reverse transcriptase polymerase chain reaction" <i>Tumor Biol.</i> 18:53-68 (1997).	
Jee	109	Hsaio et al., "Synthesis of 5'-thymidyl bis(1-aziridinyl)phosphinates as antineoplastic agents" <i>J. Med. Chem.</i> 24:887-889 (1981).	
Jee	110	Huang et al., "Active site general catalysts are not necessary for some proton transfer reactions of thymidylate synthase" <i>Biochem.</i> 36:1869-1873 (1997).	
Jee	111	Hudziak et al., "Amplified expression of the HER2/ERBB2 oncogene induces resistance to tumor necrosis factor I in NIH 3T3 cells" <i>PNAS USA</i> 85:5102-5106 (1988).	
Jee	112	Hudziak et al., "Selection for transformation and <i>met</i> protooncogene amplification in NIH 3T3 fibroblasts using tumor necrosis factor I" <i>Cell Growth &amp; Differentiation</i> 1:129-134 (1990).	
Jee	113	Husak, R. et al. "Pseudotumour of the tongue caused by herpes simplex virus type 2 in an HIV-1 infected immunosuppressed patient" <i>British J. Dermatol.</i> 139:118-121 (1998)	
Jee	114	Imai et al., "Studies on phosphorylation. IV. Selective phosphorylation of the primary hydroxyl group in nucleosides" <i>J. Org. Chem.</i> 34(6):1547-1550 (1969).	
Jee	115	Jackman et al., "Quinazoline-based thymidylate synthase inhibitors: Relationship between structural modifications and polyglutamation" <i>Anti-Cancer Drug Design</i> 10:573-589 (1995).	
Jee	116	Johnston et al., "Production and characterization of monoclonal antibodies that localize human thymidylate synthase in the cytoplasm of human cells and tissue" <i>Can. Res.</i> 51:6668-6676 (1991).	
Jee	117	Johnston, "The role of thymidylate synthase expression in prognosis and outcome of adjuvant chemotherapy in patients with rectal cancer" <i>J. Clin. Oncol.</i> 12(12):2640-2647 (1994).	
Jee	118	Kamb et al., "Cyclin-dependent kinase inhibitors and human cancer" <i>Curr. Top. Microbiol. Immunol.</i> 227:139-148 (1998).	
Jee	119	Kashani-Sabet et al., "Detection of drug resistance in human tumors by <i>in vitro</i> enzymatic amplification" <i>Can. Res.</i> 48:5775-5778 (1988).	

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## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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JAC	120	Katki, A.G. et al. "Prodrugs activated by thymidylate synthase: Treatment of tumors with deoxyuridine analogs" <i>Proc. Amer. Assoc. Cancer Res.</i> 39, Abstract No. 1275 (March 1998)	
JAC	121	Klecker et al., "Toxicity, metabolism, DNA incorporation with lack of repair, and lactate production for 1-(2'-fluoro-2'-deoxy-J-D-arabinofuranosyl)-5-iodouracil in U-937 and MOLT-4 cells" <i>Mol. Pharmacol.</i> 46:1204-1209 (1994).	
JAC	122	Knighton et al., "Structure and kinetic channelling in bifunctional dihydrofolate reductase-thymidylate synthase" <i>Nature Struct. Biol.</i> 1(3):186-194 (1994).	
JAC	123	Kobayashi et al., "Effect of hammerhead ribozyme against human thymidylate synthase on the cytotoxicity of thymidylate synthase inhibitors" <i>Jpn. J. Can. Res.</i> 86:1014-1018 (1995).	
JAC	124	Kodama, E. et al. "Evaluation of antiherpetic compounds using a gastric cancer cell line: Pronounced activity of BVDU against herpes simplex virus replication" <i>Microbiol. Immunol.</i> 40(5):359-363 (1996)	
JAC	125	Kumar et al., "Synthesis and biological evaluation of some cyclic phosphoramidate nucleoside derivatives" <i>J. Med. Chem.</i> 33(9):2368-2735 (1990).	
JAC	126	Kundu, "Synthesis and biological activities of [E]-5-(2-acylvinyl) uracils" <i>Eur. J. Med. Chem.</i> 28:473-479 (1993).	
JAC	127	Kuroboshi et al., "A facile synthesis of difluoromethylene compounds by oxidative fluorodesulfurization of dithioacetals using tetrabutylammonium dihydrogenfluoride and N-halo compounds" <i>SYNLETT</i> :909-910 (1991).	
JAC	128	Kuroboshi et al., "A facile synthesis of 1,1-difluoroalkyl ethers and carbonyl fluoride acetals by oxidative desulfurization-fluorination" <i>SYNLETT</i> :251-252 (1994).	
JAC	129	Lam, "Application of combinatorial library methods in cancer research and drug discovery" <i>Anticancer Drug Design</i> 12:145-167 (1997).	
JAC	130	Larsson, P.A., et al. "Thymidylate synthase in advanced gastrointestinal and breast cancers" <i>Acta Oncologica</i> 35(4):469-472 (1996)	
JAC	131	Lasic, "Doxorubicin in sterically stabilized liposomes" <i>Nature</i> 380:561-562 (1996).	
JAC	132	Lewis et al., "A serum-resistant cytofection for cellular delivery of antisense oligodeoxynucleotides and plasmid DNA" <i>PNAS USA</i> 93:3176-3181 (1996).	
JAC	133	Li et al., "Lack of functional retinoblastoma protein mediates increased resistance to antimetabolites in human sarcoma cell lines" <i>PNAS USA</i> 92:10436-10440 (1995).	
JAC	134	Lin et al., "Rhenium-188 hydroxyethylidene diphosphonate: A new generator-produced radiotherapeutic drug of potential value for the treatment of bone metastases" <i>Eur. J. Nucl. Med.</i> 24(6):590-595 (1997).	
JAC	135	Livak et al., "Detection of single base differences using biotinylated nucleotides with very long linker arms" <i>Nucl. Acids Res.</i> 20(18):4831-4837 (1992).	
JAC	136	Livingstone, L.R. et al., "Altered cell cycle arrest and gene amplification potential accompany loss of wild-type p53" <i>Cell</i> 70:923-935 (1992).	
JAC	137	Lönn et al., "Higher frequency of gene amplification in breast cancer patients who received adjuvant chemotherapy" <i>Cancer</i> 77(1):107-112 (1996).	
JAC	138	Lovejoy et al., "Animal models and the molecular pathology of cancer" <i>J. Pathol.</i> 181:130-135 (1997).	
JAC	139	Masters et al., "The nucleotide sequence of the cDNA coding for the human dihydrofolate reductase" <i>Gene</i> 21:59-63 (1983).	
JAC	140	McGuigan, "Aryl phosphate derivatives of AZT retain activity HIV1 in cell lines which are resistant to the action of AZT" <i>Antiviral Res.</i> 17:311-321 (1992)	
JAC	141	McGuigan, "Intracellular delivery of bioactive AZT nucleotides by aryl phosphate derivatives of AZT" <i>J. Med. Chem.</i> 36:1048-1052 (1993)	
JAC	142	McGuigan et al., "Certain phosphoramidate derivatives of dideoxy uridine (ddU) are active against HIV and successfully by-pass thymidine kinase" <i>FEBS Lett</i> 351:11-14 (1994)	
JAC	143	McGuigan, "Aryl phosphoramidate derivatives of d4T have improved anti-HIV efficacy in tissue culture and may act by the generation of a novel intracellular metabolite" <i>J. Med. Chem.</i> 39:1748-1753 (1996).	
JAC	144	McGuigan et al., "Synthesis and evaluation of some masked phosphate esters of the anti-herpetic drug 882C (netivudine) as potential antiviral agents" <i>Antiviral Chem. Chemother.</i> 9:187-197 (1998).	
JAC	145	McIntee, "Probing the mechanism of action and decomposition of amino acid phosphomonoester amidates of antiviral nucleoside prodrugs" <i>J. Med. Chem.</i> 40:3323-3331 (1997).	
JAC	146	McKay et al., "Broad spectrum aminoglycoside phosphotransferase type III from <i>Enterococcus</i> : Overexpression, purification, and substrate specificity" <i>Biochem</i> 33:6936-6944 (1994).	
JAC	147	Meden et al., "Elevated serum levels of a c-erbB-2 oncogene product in ovarian cancer patients and in pregnancy" <i>J. Can. Res. Clin. Oncol.</i> 120:378-381 (1994).	
JAC	148	Meier et al., "ADA-bypass by lipophilic cyclosal-ddAMP pro-nucleotides a second example of the efficiency of the cyclosal-concept" <i>Bioorg. Med. Chem. Lett.</i> 7(12):1577-1582 (1997).	
JAC	149	Meier et al., "Cyclic saligenyl phosphotriesters of 2',3'-dideoxy-2',3'-didehydrothymidine (d4T)- a new pro-nucleotide approach" <i>Bioorg. Med. Chem. Lett.</i> 7(2):99 (1997).	
JAC	150	Meier et al., "CycloSal-pro-nucleotides: The design and biological evaluation of a new class of lipophilic nucleotide prodrugs" <i>Int'l. Antiviral News</i> 5(10):183-185 (1997).	
JAC	151	Melton et al., "Antibody-enzyme conjugates for cancer therapy" <i>J. Natl. Can. Inst.</i> 88(3/4):153-165 (1996).	
JAC	152	Montfort et al., "Thymidylate synthase: Structure, inhibition, and strained conformations during catalysis" <i>Pharmacol. Ther.</i> 76(1-3):29-43 (1997).	
JAC	153	Montgomery et al., "Phosphonate analogue of 2'-deoxy-5-fluorouridylic acid" <i>J. Med. Chem.</i> 22(1):109-111 (1979).	
JAC	154	Morgan et al., "Tumor efficacy and bone marrow-sparing properties of TER286, a cytotoxin activated by glutathione S-transferase" <i>Can. Res.</i> 58:2568-2575 (1998).	
JAC	155	Murakami et al., "Accumulation of genetic alterations and their significance in each primary human cancer and cell line" <i>Mutat. Res.</i> 400(1-2):421-437 (1998).	

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## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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Jhe	156	Nakano et al., "Critical role of phenylalanine 34 of human dihydrofolate reductase in substrate and inhibitor binding and in catalysis" <i>Biochem.</i> 33:9945-9952 (1994).	
Jhe	157	Nooter et al., "Molecular mechanisms of multidrug resistance in cancer chemotherapy" <i>Pathol. Res. Pract.</i> 192:768-780 (1996).	
Jhe	158	Osaki et al., "5-fluorouracil (5-FU) induced apoptosis in gastric cancer cell lines: Role of the p53 gene" <i>Apoptosis</i> 2:221-226 (1997).	
Jhe	159	Oshiro, Y. et al. "Genotoxic properties of (E)-5-(2-bromovinyl)-2'-deoxyuridine (BVDU)" <i>Fund. Appl. Toxicol.</i> 18:491-498 (1992).	
Jhe	160	Pardo et al. "The incorporation of deoxyuridine monophosphate in DNA increases the sister-chromatid exchange yield" <i>Exp Cell Res.</i> 168:507-517 (1987)	
Jhe	161	Park, N.H. et al. "Chemotherapy efficacy of E-5-(2-bromovinyl)-2'-deoxyuridine for orofacial infection with herpes simplex virus type 1 in mice" <i>J. Infectious Diseases</i> 145(6):909-913 (1982)	
Jhe	162	Perry et al. "Plastic adaptation toward mutations in proteins: Structural comparison of thymidylate synthases" <i>Proteins</i> 8:315-333 (1990).	
Jhe	163	Pestalozzi et al., "Prognostic importance of thymidylate synthase expression in early breast cancer" <i>J. Clin. Oncol.</i> 15(5):1923-1931 (1997).	
Jhe	164	Peters et al., "Thymidylate synthase and drug resistance" <i>Eur. J. Can.</i> 31A(7/8):1299-1305 (1995).	
Jhe	165	Phelps et al., "Synthesis and biological activity of 5-fluoro-2'-deoxyuridine 5'-phosphorodiamidates" <i>J. Med. Chem.</i> 23:1229-1232 (1980).	
Jhe	166	Pupa et al., "The extracellular domain of the c-erbB-2 oncoprotein is released from tumor cells by proteolytic cleavage" <i>Oncogene</i> 8:2917-2923 (1993).	
Jhe	167	Roberts, "An isotopic assay for thymidylate synthetase" <i>Biochem.</i> 5(11):3546-3548 (1966).	
Jhe	168	Robins et al., "Nucleic acid related compounds. 31. Smooth and efficient palladium-copper catalyzed coupling of terminal alkynes with 5-iodouracil nucleosides" <i>Tetrahedron Lett.</i> 22:421-424 (1981).	
Jhe	169	Robins et al., "Nucleic acid related compounds. 38. Smooth and high-yield iodination and chlorination at C-5 of uracil bases and p-toluy-protected nucleosides" <i>Can. J. Chem.</i> 60:554-557 (1982).	
Jhe	170	Robins et al., "Nucleic acid compounds. 39. Efficient conversion of 5-iodo to 5-alkynyl and derived 5-substituted uracil bases and nucleosides" <i>J. Org. Chem.</i> 48:1854-1862 (1983).	
Jhe	171	Rogulski, K.R. et al. "Glioma cells transduced with an <i>Escherichia coli</i> CD/HSV-1 TK fusion gene exhibit enhanced metabolic suicide and radiosensitivity" <i>Hum. Gene Ther.</i> 8:73-85 (1997)	
Jhe	172	Roninson et al., "Amplification of specific DNA sequences correlates with multi-drug resistance in chinese hamster cells" <i>Nature</i> 309:626-628 (1984).	
Jhe	173	Ruth et al., "C-5 substituted pyrimidine nucleosides. 1. Synthesis of C-5 allyl, propyl, and propenyl uracil and cytosine nucleosides via organopalladium intermediates" <i>J. Org. Chem.</i> 43(14):2870-2876 (1978).	
Jhe	174	Santi, "Perspectives on the design and biochemical pharmacology of inhibitors of thymidylate synthetase" <i>J. Med. Chem.</i> 28(2):103-111 (1980).	
Jhe	175	Sastry et al., "Membrane-permeable dideoxyuridine 5'-monophosphate analogue inhibits human immunodeficiency virus infection" <i>Mol. Pharmacol.</i> 41:441-445 (1992).	
Jhe	176	Sauter et al., "Heterogeneity of <i>erbB-2</i> gene amplification in bladder cancer" <i>Can. Res.</i> 53:2199-2203 (1993).	
Jhe	177	Schiffer et al., "Crystal structure of human thymidylate synthase: A structural mechanism for guiding substrates into the active site" <i>Biochem.</i> 34:16279-16287 (1995).	
Jhe	178	Schimke, "Gene amplification in cultured cells" <i>J. Biol. Chem.</i> 263(13):5989-5992 (1988).	
Jhe	179	Segovia, "Leishmania gene amplification: A mechanism of drug resistance" <i>Annals Tropical Med. Parasitol.</i> 88(2):123-130 (1994).	
Jhe	180	Shepard et al., "Resistance of tumor cells to tumor necrosis factor" <i>J. Clin. Immunol.</i> 8(5):333-341 (1988).	
Jhe	181	Simon, "Cell biological mechanisms of multidrug resistance in tumors" <i>PNAS USA</i> 91:3497-3504 (1994).	
Jhe	182	Singh et al., "Studies on the preparation and isomeric composition of 186Re- and 188Re-pentavalent rhenium dimercaptosuccinic acid complex" <i>Nucl. Med. Commun.</i> 14:197-203 (1993).	
Jhe	183	Slamon et al., "Human breast cancer: Correlation of relapse and survival with amplification of the HER-2/ <i>neu</i> oncogene" <i>Science</i> 235:177-182 (1987).	
Jhe	184	Slamon et al., "Studies of the HER-2/ <i>neu</i> proto-oncogene in human breast and ovarian cancer" <i>Science</i> 244:707-712 (1989).	
Jhe	185	Smith et al., "Regulation and mechanisms of gene amplification" <i>Phil. Trans. Royal Soc. Lond. B</i> 347:49-56 (1995).	
Jhe	186	Snydman et al., "Analysis of trends in antimicrobial resistance patterns among clinical isolates of <i>Bacteroides fragilis</i> group species from 1990 to 1994" <i>Clin. Infectious Diseases</i> 23(Suppl. 1):S54-S65 (1996).	
Jhe	187	Staschke, K.A. et al. "The in vitro anti-hepatitis B virus activity of FIAU [1-(2'-deoxy-2'-fluoro-1-β-D-arabinofuranosyl-5-iodo)uracil] is selective, reversible, and determined, at least in part, by the host cell" <i>Antiviral Res.</i> 23:45-61 (1994)	
Jhe	188	Stout et al., "Structure-based design of inhibitors specific for bacterial thymidylate synthase" <i>Biochem.</i> 38:1607-1617 (1999).	
Jhe	189	Stühlinger et al., "Clinical therapy and HER-2 oncogene amplification in breast cancer: Chemo-vs radiotherapy" <i>J. Steroid Biochem. Molec. Biol.</i> 49(1):39-42 (1994).	
Jhe	190	Sugarman et al., "Recombinant human tumor necrosis factor- $\alpha$ . Effects on proliferation of normal and transformed cells in vitro" <i>Science</i> 230(4728):943-945 (1985).	
Jhe	191	Sukumar et al., "Specific patterns of oncogene activation in transplacentally induced tumors" <i>PNAS USA</i> 87:718-722 (1990).	

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Application Number	09/782,721
Filing Date	February 12, 2001
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 -1653-
Examiner Name	L. Crane
Attorney Docket Number	NB 2004.02

## U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number - Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
me	B 1	US-4,668,777	05-26-87	Caruthers et al.	
me	B 2	US-4,963,263	10-16-90	Kauver	
me	B 3	US-4,963,533	10-16-90	De Clercq et al.	
me	B 4	US-5,116,822	05-26-92	De Clercq et al.	
me	B 5	US-5,133,866	07-28-92	Kauver	
me	B 6	US-5,137,724	08-11-92	Balzarini et al.	
me	B 7	US-5,217,869	06-08-93	Kauver	
me	B 8	US-5,300,425	04-05-94	Kauver	
me	B 9	US-5,338,659	08-16-94	Kauver, et al.	
me	B 10	US-5,430,148	07-04-95	Webber, et al.	
me	B 11	US-5,433,955	07-18-95	Bredehorst et al.	
me	B 12	US-5,516,631	05-14-96	Frisch	
me	B 13	US-5,527,900	06-18-96	Balzarini et al.	
me	B 14	US-5,596,018	01-21-97	Baba et al.	
me	B 15	US-5,733,896	03-31-98	Holy et al.	
me	B 16	US-5,968,910	10-19-99	Balzarini	
me	B 17	US-6,057,305	05-02-00	Holy et al.	

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## FOREIGN PATENT DOCUMENTS

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me	B 18	DE 32 29 169 A1	02-09-84	De Clercq et al.		
me	B 19	EP 0 311 107 A2	04-12-89	Stichting REGA VZW		
me	B 20	EP 0 311 108A2	04-12-89	Stichting REGA VZW		
me	B 21	EP 0 316 592	05-24-89	Stichting REGA VZW		
me	B 22	WO 90/03978	04-19-90	Stichting REGA VZW		
me	B 23	WO 92/19767	11-12-92	Terrapin Technologies, Inc.		

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				Filing Date	February 12, 2001
				First Named Inventor	H. Michael SHEPARD
				Art Unit	1623 -4653-
				Examiner Name	L. Crane
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FOREIGN PATENT DOCUMENTS					
Me	B 24	WO 95/09865	04-13-95	Terrapin Technologies, Inc.	
Me	B 25	WO 96/40739	12-19-96	Terrapin Technologies, Inc.	
Me	B 26	WO 97/25342	07-17-97	Terrapin Technologies, Inc.	
Me	B 27	WO 97/49717	12-31-97	Balzarini et al.	
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Me	C 1	BAJETTA, E. et al. "A pilot safety study of capecitabine, a new oral fluoropyrimidine, in patients with advanced neoplastic disease" <i>Tumor</i> (1996) 82:450-452		
Me	C 2	CODERRE, J.A. et al. "Mechanism of action of 2',5-difluoro-1-arabinosyluracil" <i>J. Med. Chem.</i> (1983) 26(8):1149-1152		
Me	C 3	MEAD, J.A.R. et al. "Pharmacologic aspects of homofolate derivatives in relation to amethopterin-resistant murine leukemia" <i>Cancer Res.</i> (November 1966) 26(1):2374-2379 (November, 1966).		
Me	C 4	NICHOL, C.A. and M.T. HAKALA "Comparative growth-inhibitory activity of homofolic acid against cell lines sensitive and resistant to amethopterin" <i>Biochem. Pharmacol.</i> (October 1966) 15(10):1621-1623 (October, 1966).		
Me	C 5	RODE, W. "Specificity of thymidylate synthase inactivation by 4,5-bisubstituted dUMP analogues" <i>M. Nencki Inst. Exp. Biol., Acta Biochimica Polonica</i> (1993) 40(3):363-368		
Me	C 6	SATYAM, A. et al. "Design, synthesis, and evaluation of latent alkylating agents activated by glutathione S-transferase" <i>J. Med. Chem.</i> (1996) 39:1736-1747		
Me	C 7	WATAYA, Y. et al. "Interaction of thymidylate synthetase with 5-nitro-2'-deoxyuridylate" <i>J. Biol. Chem.</i> (June 1980) 255(12):5538-5544		

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